

SEQUENCE LISTING

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<120> METAL IMPLANT COATED WITH OSTEOINDUCTIVE PROTEINS AND METHODS FOR ITS MANUFACTURE

<130> 009848-0314856

<140> TO BE ASSIGNED

<141> HEREWITH

<150> PCT/EP03/07439

<151> 2003-07-09

<160> 6

<170> PatentIn version 3.1

<210> 1

<211> 396

<212> PRT

<213> Homo sapiens

<400> 1

Met Val Ala Gly Thr Arg Cys Leu Leu Ala Leu Leu Leu Pro Gln Val
1 5 10 15

Leu Leu Gly Gly Ala Ala Gly Leu Val Pro Glu Leu Gly Arg Arg Lys
20 25 30

Phe Ala Ala Ala Ser Ser Gly Arg Pro Ser Ser Gln Pro Ser Asp Glu
35 40 45

Val Leu Ser Glu Phe Glu Leu Arg Leu Leu Ser Met Phe Gly Leu Lys
50 55 60

Gln Arg Pro Thr Pro Ser Arg Asp Ala Val Val Pro Pro Tyr Met Leu
65 70 75 80

Asp Leu Tyr Arg Arg His Ser Gly Gln Pro Gly Ser Pro Ala Pro Asp
85 90 95

His Arg Leu Glu Arg Ala Ala Ser Arg Ala Asn Thr Val Arg Ser Phe
100 105 110

His His Glu Glu Ser Leu Glu Glu Leu Pro Glu Thr Ser Gly Lys Thr
115 120 125

Thr Arg Arg Phe Phe Phe Asn Leu Ser Ser Ile Pro Thr Glu Glu Phe
 130 135 140

Ile Thr Ser Ala Glu Leu Gln Val Phe Arg Glu Gln Met Gln Asp Ala
 145 150 155 160

Leu Gly Asn Asn Ser Ser Phe His His Arg Ile Asn Ile Tyr Glu Ile
 165 170 175

Ile Lys Pro Ala Thr Ala Asn Ser Lys Phe Pro Val Thr Arg Leu Leu
 180 185 190

Asp Thr Arg Leu Val Asn Gln Asn Ala Ser Arg Trp Glu Ser Phe Asp
 195 200 205

Val Thr Pro Ala Val Met Arg Trp Thr Ala Gln Gly His Ala Asn His
 210 215 220

Gly Phe Val Val Glu Val Ala His Leu Glu Glu Lys Gln Gly Val Ser
 225 230 235 240

Lys Arg His Val Arg Ile Ser Arg Ser Leu His Gln Asp Glu His Ser
 245 250 255

Trp Ser Gln Ile Arg Pro Leu Leu Val Thr Phe Gly His Asp Gly Lys
 260 265 270

Gly His Pro Leu His Lys Arg Glu Lys Arg Gln Ala Lys His Lys Gln
 275 280 285

Arg Lys Arg Leu Lys Ser Ser Cys Lys Arg His Pro Leu Tyr Val Asp
 290 295 300

Phe Ser Asp Val Gly Trp Asn Asp Trp Ile Val Ala Pro Pro Gly Tyr
 305 310 315 320

His Ala Phe Tyr Cys His Gly Glu Cys Pro Phe Pro Leu Ala Asp His
 325 330 335

Leu Asn Ser Thr Asn His Ala Ile Val Gln Thr Leu Val Asn Ser Val
 340 345 350

Asn Ser Lys Ile Pro Lys Ala Cys Cys Val Pro Thr Glu Leu Ser Ala
 355 360 365

Ile Ser Met Leu Tyr Leu Asp Glu Asn Glu Lys Val Val Leu Lys Asn
 370 375 380

Tyr Gln Asp Met Val Val Glu Gly Cys Gly Cys Arg
 385 390 395

<210> 2
 <211> 431
 <212> PRT
 <213> Homo Sapiens

<400> 2

Met His Val Arg Ser Leu Arg Ala Ala Ala Pro His Ser Phe Val Ala
 1 5 10 15

Leu Trp Ala Pro Leu Phe Leu Leu Arg Ser Ala Leu Ala Asp Phe Ser
 20 25 30

Leu Asp Asn Glu Val His Ser Ser Phe Ile His Arg Arg Leu Arg Ser
 35 40 45

Gln Glu Arg Arg Glu Met Gln Arg Glu Ile Leu Ser Ile Leu Gly Leu
 50 55 60

Pro His Arg Pro Arg Pro His Leu Gln Gly Lys His Asn Ser Ala Pro
 65 70 75 80

Met Phe Met Leu Asp Leu Tyr Asn Ala Met Ala Val Glu Glu Gly Gly
 85 90 95

Gly Pro Gly Gly Gln Gly Phe Ser Tyr Pro Tyr Lys Ala Val Phe Ser
 100 105 110

Thr Gln Gly Pro Pro Leu Ala Ser Leu Gln Asp Ser His Phe Leu Thr
 115 120 125

Asp Ala Asp Met Val Met Ser Phe Val Asn Leu Val Glu His Asp Lys
 130 135 140

Glu Phe Phe His Pro Arg Tyr His His Arg Glu Phe Arg Phe Asp Leu
 145 150 155 160

Ser Lys Ile Pro Glu Gly Glu Ala Val Thr Ala Ala Glu Phe Arg Ile
 165 170 175

Tyr Lys Asp Tyr Ile Arg Glu Arg Phe Asp Asn Glu Thr Phe Arg Ile
180 185 190

Ser Val Tyr Gln Val Leu Gln Glu His Leu Gly Arg Glu Ser Asp Leu
195 200 205

Phe Leu Leu Asp Ser Arg Thr Leu Trp Ala Ser Glu Glu Gly Trp Leu
210 215 220

Val Phe Asp Ile Thr Ala Thr Ser Asn His Trp Val Val Asn Pro Arg
225 230 235 240

His Asn Leu Gly Leu Gln Leu Ser Val Glu Thr Leu Asp Gly Gln Ser
245 250 255

Ile Asn Pro Lys Leu Ala Gly Leu Ile Gly Arg His Gly Pro Gln Asn
260 265 270

Lys Gln Pro Phe Met Val Ala Phe Phe Lys Ala Thr Glu Val His Phe
275 280 285

Arg Ser Ile Arg Ser Thr Gly Ser Lys Gln Arg Ser Gln Asn Arg Ser
290 295 300

Lys Thr Pro Lys Asn Gln Glu Ala Leu Arg Met Ala Asn Val Ala Glu
305 310 315 320

Asn Ser Ser Ser Asp Gln Arg Gln Ala Cys Lys Lys His Glu Leu Tyr
325 330 335

Val Ser Phe Arg Asp Leu Gly Trp Gln Asp Trp Ile Ile Ala Pro Glu
340 345 350

Gly Tyr Ala Ala Tyr Tyr Cys Glu Gly Glu Cys Ala Phe Pro Leu Asn
355 360 365

Ser Tyr Met Asn Ala Thr Asn His Ala Ile Val Gln Thr Leu Val His
370 375 380

Phe Ile Asn Pro Glu Thr Val Pro Lys Pro Cys Cys Ala Pro Thr Gln
385 390 395 400

Leu Asn Ala Ile Ser Val Leu Tyr Phe Asp Asp Ser Ser Asn Val Ile
405 410 415

Leu Lys Lys Tyr Arg Asn Met Val Val Arg Ala Cys Gly Cys His
 420 425 430

<210> 3
 <211> 501
 <212> PRT
 <213> Homo Sapiens

<400> 3

Met Arg Leu Pro Lys Leu Leu Thr Phe Leu Leu Trp Tyr Leu Ala Trp
 1 5 10 15

Leu Asp Leu Glu Phe Ile Cys Thr Val Leu Gly Ala Pro Asp Leu Gly
 20 25 30

Gln Arg Pro Gln Gly Ser Arg Pro Gly Leu Ala Lys Ala Glu Ala Lys
 35 40 45

Glu Arg Pro Pro Leu Ala Arg Asn Val Phe Arg Pro Gly Gly His Ser
 50 55 60

Tyr Gly Gly Gly Ala Thr Asn Ala Asn Ala Arg Ala Lys Gly Gly Thr
 65 70 75 80

Gly Gln Thr Gly Gly Leu Thr Gln Pro Lys Lys Asp Glu Pro Lys Lys
 85 90 95

Leu Pro Pro Arg Pro Gly Gly Pro Glu Pro Lys Pro Gly His Pro Pro
 100 105 110

Gln Thr Arg Gln Ala Thr Ala Arg Thr Val Thr Pro Lys Gly Gln Leu
 115 120 125

Pro Gly Gly Lys Ala Pro Pro Lys Ala Gly Ser Val Pro Ser Ser Phe
 130 135 140

Leu Leu Lys Lys Ala Arg Glu Pro Gly Pro Pro Arg Glu Pro Lys Glu
 145 150 155 160

Pro Phe Arg Pro Pro Pro Ile Thr Pro His Glu Tyr Met Leu Ser Leu
 165 170 175

Tyr Arg Thr Leu Ser Asp Ala Asp Arg Lys Gly Gly Asn Ser Ser Val
 180 185 190

Lys Leu Glu Ala Gly Leu Ala Asn Thr Ile Thr Ser Phe Ile Asp Lys
 195 200 205

Gly Gln Asp Asp Arg Gly Pro Val Val Arg Lys Gln Arg Tyr Val Phe
 210 215 220

Asp Ile Ser Ala Leu Glu Lys Asp Gly Leu Leu Gly Ala Glu Leu Arg
 225 230 235 240

Ile Leu Arg Lys Lys Pro Ser Asp Thr Ala Lys Pro Ala Val Pro Arg
 245 250 255

Ser Arg Arg Ala Ala Gln Leu Lys Leu Ser Ser Cys Pro Ser Gly Arg
 260 265 270

Gln Pro Ala Ala Leu Leu Asp Val Arg Ser Val Pro Gly Leu Asp Gly
 275 280 285

Ser Gly Trp Glu Val Phe Asp Ile Trp Lys Leu Phe Arg Asn Phe Lys
 290 295 300

Asn Ser Ala Gln Leu Cys Leu Glu Leu Glu Ala Trp Glu Arg Gly Arg
 305 310 315 320

Thr Val Asp Leu Arg Gly Leu Gly Phe Asp Arg Ala Ala Arg Gln Val
 325 330 335

His Glu Lys Ala Leu Phe Leu Val Phe Gly Arg Thr Lys Lys Arg Asp
 340 345 350

Leu Phe Phe Asn Glu Ile Lys Ala Arg Ser Gly Gln Asp Asp Lys Thr
 355 360 365

Val Tyr Glu Tyr Leu Phe Ser Gln Arg Arg Lys Arg Arg Ala Pro Leu
 370 375 380

Ala Thr Arg Gln Gly Lys Arg Pro Ser Lys Asn Leu Lys Ala Arg Cys
 385 390 395 400

Ser Arg Lys Ala Leu His Val Asn Phe Lys Asp Met Gly Trp Asp Asp
 405 410 415

Trp Ile Ile Ala Pro Leu Glu Tyr Glu Ala Phe His Cys Glu Gly Leu
 420 425 430

Cys Glu Phe Pro Leu Arg Ser His Leu Glu Pro Thr Asn His Ala Val
 435 440 445

Ile Gln Thr Leu Met Asn Ser Met Asp Pro Glu Ser Thr Pro Pro Thr
 450 455 460

Cys Cys Val Pro Thr Arg Leu Ser Pro Ile Ser Ile Leu Phe Ile Asp
 465 470 475 480

Ser Ala Asn Asn Val Val Tyr Lys Gln Tyr Glu Asp Met Val Val Glu
 485 490 495

Ser Cys Gly Cys Arg
 500

<210> 4
 <211> 373
 <212> PRT
 <213> Homo Sapiens

<400> 4

Leu Val Pro Glu Leu Gly Arg Arg Lys Phe Ala Ala Ala Ser Ser Gly
 1 5 10 15

Arg Pro Ser Ser Gln Pro Ser Asp Glu Val Leu Ser Glu Phe Glu Leu
 20 25 30

Arg Leu Leu Ser Met Phe Gly Leu Lys Gln Arg Pro Thr Pro Ser Arg
 35 40 45

Asp Ala Val Val Pro Pro Tyr Met Leu Asp Leu Tyr Arg Arg His Ser
 50 55 60

Gly Gln Pro Gly Ser Pro Ala Pro Asp His Arg Leu Glu Arg Ala Ala
 65 70 75 80

Ser Arg Ala Asn Thr Val Arg Ser Phe His His Glu Glu Ser Leu Glu
 85 90 95

Glu Leu Pro Glu Thr Ser Gly Lys Thr Thr Arg Arg Phe Phe Phe Asn
 100 105 110

Leu Ser Ser Ile Pro Thr Glu Glu Phe Ile Thr Ser Ala Glu Leu Gln
 115 120 125

Val Phe Arg Glu Gln Met Gln Asp Ala Leu Gly Asn Asn Ser Ser Phe
130 135 140
His His Arg Ile Asn Ile Tyr Glu Ile Ile Lys Pro Ala Thr Ala Asn
145 150 155 160
Ser Lys Phe Pro Val Thr Arg Leu Leu Asp Thr Arg Leu Val Asn Gln
165 170 175
Asn Ala Ser Arg Trp Glu Ser Phe Asp Val Thr Pro Ala Val Met Arg
180 185 190
Trp Thr Ala Gln Gly His Ala Asn His Gly Phe Val Val Glu Val Ala
195 200 205
His Leu Glu Glu Lys Gln Gly Val Ser Lys Arg His Val Arg Ile Ser
210 215 220
Arg Ser Leu His Gln Asp Glu His Ser Trp Ser Gln Ile Arg Pro Leu
225 230 235 240
Leu Val Thr Phe Gly His Asp Gly Lys Gly His Pro Leu His Lys Arg
245 250 255
Glu Lys Arg Gln Ala Lys His Lys Gln Arg Lys Arg Leu Lys Ser Ser
260 265 270
Cys Lys Arg His Pro Leu Tyr Val Asp Phe Ser Asp Val Gly Trp Asn
275 280 285
Asp Trp Ile Val Ala Pro Pro Gly Tyr His Ala Phe Tyr Cys His Gly
290 295 300
Glu Cys Pro Phe Pro Leu Ala Asp His Leu Asn Ser Thr Asn His Ala
305 310 315 320
Ile Val Gln Thr Leu Val Asn Ser Val Asn Ser Lys Ile Pro Lys Ala
325 330 335
Cys Cys Val Pro Thr Glu Leu Ser Ala Ile Ser Met Leu Tyr Leu Asp
340 345 350
Glu Asn Glu Lys Val Val Leu Lys Asn Tyr Gln Asp Met Val Val Glu
355 360 365

Gly Cys Gly Cys Arg
370

<210> 5
<211> 398
<212> PRT
<213> Homo Sapiens

<400> 5

Met Gly Ser Ser His His His His His His Ser Ser Gly Leu Val Pro
1 5 10 15

Arg Gly Ser His Met Gly Ala Ala Gly Leu Val Pro Glu Leu Gly Arg
20 25 30

Arg Lys Phe Ala Ala Ala Ser Ser Gly Arg Pro Ser Ser Gln Pro Ser
35 40 45

Asp Glu Val Leu Ser Glu Phe Glu Leu Arg Leu Leu Ser Met Phe Gly
50 55 60

Leu Lys Gln Arg Pro Thr Pro Ser Arg Asp Ala Val Val Pro Pro Tyr
65 70 75 80

Met Leu Asp Leu Tyr Arg Arg His Ser Gly Gln Pro Gly Ser Pro Ala
85 90 95

Pro Asp His Arg Leu Glu Arg Ala Ala Ser Arg Ala Asn Thr Val Arg
100 105 110

Ser Phe His His Glu Glu Ser Leu Glu Glu Leu Pro Glu Thr Ser Gly
115 120 125

Lys Thr Thr Arg Arg Phe Phe Phe Asn Leu Ser Ser Ile Pro Thr Glu
130 135 140

Glu Phe Ile Thr Ser Ala Glu Leu Gln Val Phe Arg Glu Gln Met Gln
145 150 155 160

Asp Ala Leu Gly Asn Asn Ser Ser Phe His His Arg Ile Asn Ile Tyr
165 170 175

Glu Ile Ile Lys Pro Ala Thr Ala Asn Ser Lys Phe Pro Val Thr Arg
180 185 190

Leu Leu Asp Thr Arg Leu Val Asn Gln Asn Ala Ser Arg Trp Glu Ser
 195 200 205

Phe Asp Val Thr Pro Ala Val Met Arg Trp Thr Ala Gln Gly His Ala
 210 215 220

Asn His Gly Phe Val Val Glu Val Ala His Leu Glu Glu Lys Gln Gly
 225 230 235 240

Val Ser Lys Arg His Val Arg Ile Ser Arg Ser Leu His Gln Asp Glu
 245 250 255

His Ser Trp Ser Gln Ile Arg Pro Leu Leu Val Thr Phe Gly His Asp
 260 265 270

Gly Lys Gly His Pro Leu His Lys Arg Glu Lys Arg Gln Ala Lys His
 275 280 285

Lys Gln Arg Lys Arg Leu Lys Ser Ser Cys Lys Arg His Pro Leu Tyr
 290 295 300

Val Asp Phe Ser Asp Val Gly Trp Asn Asp Trp Ile Val Ala Pro Pro
 305 310 315 320

Gly Tyr His Ala Phe Tyr Cys His Gly Glu Cys Pro Phe Pro Leu Ala
 325 330 335

Asp His Leu Asn Ser Thr Asn His Ala Ile Val Gln Thr Leu Val Asn
 340 345 350

Ser Val Asn Ser Lys Ile Pro Lys Ala Cys Cys Val Pro Thr Glu Leu
 355 360 365

Ser Ala Ile Ser Met Leu Tyr Leu Asp Glu Asn Glu Lys Val Val Leu
 370 375 380

Lys Asn Tyr Gln Asp Met Val Val Glu Gly Cys Gly Cys Arg
 385 390 395

<210> 6
 <211> 501
 <212> PRT
 <213> Homo Sapiens

<400> 6

Met	Arg	Leu	Pro	Lys	Leu	Leu	Thr	Phe	Leu	Leu	Trp	Tyr	Leu	Ala	Trp
1				5					10					15	
Leu	Asp	Leu	Glu	Phe	Ile	Cys	Thr	Val	Leu	Gly	Ala	Pro	Asp	Leu	Gly
			20					25					30		
Gln	Arg	Pro	Gln	Gly	Thr	Arg	Pro	Gly	Leu	Ala	Lys	Ala	Glu	Ala	Lys
		35					40					45			
Glu	Arg	Pro	Pro	Leu	Ala	Arg	Asn	Val	Phe	Arg	Pro	Gly	Gly	His	Ser
	50					55					60				
Tyr	Gly	Gly	Gly	Ala	Thr	Asn	Ala	Asn	Ala	Arg	Ala	Lys	Gly	Gly	Thr
65					70					75					80
Gly	Gln	Thr	Gly	Gly	Leu	Thr	Gln	Pro	Lys	Lys	Asp	Glu	Pro	Lys	Lys
				85					90					95	
Leu	Pro	Pro	Arg	Pro	Gly	Gly	Pro	Glu	Pro	Lys	Pro	Gly	His	Pro	Pro
			100					105					110		
Gln	Thr	Arg	Gln	Ala	Thr	Ala	Arg	Thr	Val	Thr	Pro	Lys	Gly	Gln	Leu
		115					120					125			
Pro	Gly	Gly	Lys	Ala	Pro	Pro	Lys	Ala	Gly	Ser	Val	Pro	Ser	Ser	Phe
	130						135				140				
Leu	Leu	Lys	Lys	Ala	Arg	Glu	Pro	Gly	Pro	Pro	Arg	Glu	Pro	Lys	Glu
145					150					155					160
Pro	Phe	Arg	Pro	Pro	Pro	Ile	Thr	Pro	His	Glu	Tyr	Met	Leu	Ser	Leu
				165					170					175	
Tyr	Arg	Thr	Leu	Ser	Asp	Ala	Asp	Arg	Lys	Gly	Gly	Asn	Ser	Ser	Val
			180					185					190		
Lys	Leu	Glu	Ala	Gly	Leu	Ala	Asn	Thr	Ile	Thr	Ser	Phe	Ile	Asp	Lys
		195					200					205			

Gly Gln Asp Asp Arg Gly Pro Val Val Arg Lys Gln Arg Tyr Val Phe
 210 215 220

Asp Ile Ser Ala Leu Glu Lys Asp Gly Leu Leu Gly Ala Glu Leu Arg
 225 230 235 240

Ile Leu Arg Lys Lys Pro Ser Asp Thr Ala Lys Pro Ala Ala Pro Gly
 245 250 255

Gly Gly Arg Ala Ala Gln Leu Lys Leu Ser Ser Cys Pro Ser Gly Arg
 260 265 270

Gln Pro Ala Ser Leu Leu Asp Val Arg Ser Val Pro Gly Leu Asp Gly
 275 280 285

Ser Gly Trp Glu Val Phe Asp Ile Trp Lys Leu Phe Arg Asn Phe Lys
 290 295 300

Asn Ser Ala Gln Leu Cys Leu Glu Leu Glu Ala Trp Glu Arg Gly Arg
 305 310 315 320

Ala Val Asp Leu Arg Gly Leu Gly Phe Asp Arg Ala Ala Arg Gln Val
 325 330 335

His Glu Lys Ala Leu Phe Leu Val Phe Gly Arg Thr Lys Lys Arg Asp
 340 345 350

Leu Phe Phe Asn Glu Ile Lys Ala Arg Ser Gly Gln Asp Asp Lys Thr
 355 360 365

Val Tyr Glu Tyr Leu Phe Ser Gln Arg Arg Lys Arg Arg Ala Pro Leu
 370 375 380

Ala Thr Arg Gln Gly Lys Arg Pro Ser Lys Asn Leu Lys Ala Arg Cys
 385 390 395 400

Ser Arg Lys Ala Leu His Val Asn Phe Lys Asp Met Gly Trp Asp Asp
 405 410 415

Trp Ile Ile Ala Pro Leu Glu Tyr Glu Ala Phe His Cys Glu Gly Leu
 420 425 430

Cys Glu Phe Pro Leu Arg Ser His Leu Glu Pro Thr Asn His Ala Val
 435 440 445

Ile Gln Thr Leu Met Asn Ser Met Asp Pro Glu Ser Thr Pro Pro Thr
450 455 460

Cys Cys Val Pro Thr Arg Leu Ser Pro Ile Ser Ile Leu Phe Ile Asp
465 470 475 480

Ser Ala Asn Asn Val Val Tyr Lys Gln Tyr Glu Asp Met Val Val Glu
485 490 495

Ser Cys Gly Cys Arg
500